COMPOSITIONS AND METHODS FOR MODULATING PHYSIOLOGY OF EPITHELIAL JUNCTIONAL ADHESION MOLECULES FOR ENHANCED MUCOSAL DELIVERY OF THERAPEUTIC COMPOUNDS

ABSTRACT OF THE DISCLOSURE

Compositions and methods are provided that include a biologically active agent and a permeabilizing agent effective to enhance mucosal delivery of the biologically active agent in a mammalian subject. The permeabilizing agent reversibly enhances mucosal epithelial paracellular transport, typically by modulating epithelial junctional structure and/or physiology at a mucosal epithelial surface in the subject. This effect typically involves inhibition by the permeabilizing agent of homotypic or heterotypic binding between epithelial membrane adhesive proteins of neighboring epithelial cells. Target proteins for this blockade of homotypic or heterotypic binding can be selected from various related junctional adhesion molecules (JAMs), occludins, or claudins. The permeabilizing agent is typically a peptide or peptide analog or mimetic, often selected or derived from an extracellular domain of a mammalian JAM, occludin or claudin protein.